

Evaluation of CPT-11 in combination with doxorubicin against pancreatic ductal adenocarcinoma PO3 on B6D2F₁ female mice BCM-887 (10.30.96-02.27.97)

Agent (batch)	Route	Dosage in mg/kg/dose	Schedule In days	Total dose in mg/kg	Fraction of HDT	Drug death (days of death)	Average body weight change in % per mouse at nadir (day of nadir)	Median tumor weight in mg on day 16 (range)	T/C in % day 16	Time for median tumor to reach 1000 mg in days	T-C in days	log cell kill total	Tumor free survivors day 120	Comments	
CPT-11	p.o. 0.2 ml	100.8	6-9	806.4	1	0/5	-16.0 (13)	75 (0-126)	8	26.2	9.8	1.3	0/5	HDT active	
		62.5	(2x/day)	500.0		0/5	-3.9 (13)	126 (32-340)	14	25.7	9.3	1.2	0/5	Active	
		38.8		310.4		0/5	-3.5 (13)	202 (0-1162)	22	20.4	4.0	0.5	0/5	Inactive	
Doxorubicin	i.v. 0.2 ml	10.0	6-9	20.0	1	0/5	-14.1 (15)	0 (0-0)	0						
		6.2		12.4		0/5	-4.4 (13)	126 (0-214)	14	25.9	9.5	1.2	0/5	HDT highly active	
		3.8		7.6		0/5	-5.1 (15)	382 (32-546)	42	23.9	7.5	1.0	0/5	Active	
Doxorubicin CPT-11	iv/0.2ml po/0.2ml	5.0	6-9	10.0	0.5	0/5	-10.3 (13)	0 (0-0)	0						
		80.6	6-9	644.8	0.8	1.3	0/5	-6.9 (13)	0 (0-0)	0	52.0	35.6	4.7	1/5	Highly active
		4.1	(2x/day)	8.2	0.41	1.06	0/5	-2.5 (8)	0 (0-0)	0	39.9	23.5	3.1	0/5	Highly active
		65.5		524.0	0.65	0/5	-3.9 (13)	72 (0-126)	8	28.7	12.3	1.6	0/5	Active	
		3.1		6.2	0.31	0/5	-1.8 (14)	336 (270-942)	37	20.5	4.1	0.5	0/5	Inactive	
		50.4		403.2	0.50	0.81	0/5								
		2.2		4.4	0.22	0/5									
		35.3		282.4	0.35	0.57	0/5								
		1.2		2.4	0.12	0/5									
Control		20.1		160.8	0.20	0.32									
		918 (343-1444)										16.4			0/10

Tumor doubling time = 2.3 days. Mice average weight: CPT-11 = 24.39 g, doxorubicin = 25.26 g, combination = 23.50 g. The 2 administrations of CPT-11 were performed 4 hours apart.

Abbreviation used: HDT = highest dose tested.

Figure 1